

Day : Wednesday

Date: 9/10/2003

Time: 09:41:49

PALM INTRANET**Inventor Name Search Result**

Your Search was:

Last Name = STUDER

First Name = LORENZ

Application#	Patent#	Status	Date Filed	Title	Inventor Name
<u>60285654</u>	Not Issued	159	04/20/2001	GENERATION OF DIFFERENTIATED TISSUE FROM NUCLEAR TRANSFER EMBRYONIC SYSTEM CELLS AND METHODS OF USE	STUDER, LORENZ
<u>60201005</u>	Not Issued	159	05/01/2000	DERIVATION OF MIDBRAIN DOPAMINERGIC NEURONS FROM EMBRYONIC STEM CELLS	STUDER, LORENZ
<u>60093991</u>	Not Issued	159	07/24/1998	CELL EXPANSION SYSTEM FOR USE IN NEURAL TRANSPLANTATION	STUDER, LORENZ
<u>10462896</u>	Not Issued	019	06/13/2003	LOW OXYGEN CULTURING OF CENTRAL NERVOUS SYSTEM PROGENITOR CELLS	STUDER, LORENZ
<u>10258975</u>	Not Issued	030	04/08/2003	DERIVATION OF MIDBRAIN DOPAMINERGIC NEURONS FROM EMBRYONIC STEM CELLS	STUDER, LORENZ
<u>10127740</u>	Not Issued	030	04/22/2002	GENERATION OF DIFFERENTIATED TISSUE FROM NUCLEAR TRANSFER EMBRYONIC STEM CELLS AND METHODS OF USE	STUDER, LORENZ
<u>09744384</u>	Not Issued	071	03/16/2001	CELL EXPANSION SYSTEM FOR USE IN NEURAL TRANSPLANTATION	STUDER, LORENZ
<u>09425462</u>	<u>6610540</u>	150	10/22/1999	LOW OXYGEN CULTURING OF CENTRAL NERVOUS SYSTEM PROGENITOR CELLS	STUDER, LORENZ

Inventor Search Completed: No Records to Display.

**Search Another:
Inventor**

Last Name

STUDER

First Name

LORENZ

Search

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L7 ANSWER 32 OF 108 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2001:582027 CAPLUS
 DOCUMENT NUMBER: 135:149603
 TITLE: Generation of dopaminergic neurons from human nervous system stem cells
 INVENTOR(S): Zobel, Rita; Levesque, Michel F.
 PATENT ASSIGNEE(S): Neurogeneration, Inc., USA
 SOURCE: PCT Int. Appl., 15 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057191	A1	20010809	WO 2001-US1564	20010116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6395546	B1	20020528	US 2000-490569	20000201

PRIORITY APPLN. INFO.: US 2000-490569 A 20000201

AB The present invention relates to methods for generating **dopaminergic** neurons in vitro from embryonic and adult **central nervous system** cells. Specifically, these cells are isolated, cultured in vitro and stimulated to **differentiate** into **dopaminergic** neurons by down-regulating COUP-TFI and/or COUP-TFII expression or increasing NOT1 expression. These newly generated **dopaminergic** neurons may serve as an excellent source for cell replacement therapy in neurological disorders in which the **dopaminergic** system is compromised.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Biblio	Desc	Claims	Drawing	Return
◀◀	1/80 - Biblio	▶▶		



LOW OXYGEN CULTURING OF CENTRAL NERVOUS SYSTEM PROGENITOR CELLS

RELATED APPLICATIONS

5 The present application is a continuation-in-part of U.S. Application number
09/195,569 filed November 18, 1998. The entire text of the above referenced
application is incorporated herein by reference without prejudice or disclaimer.

FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

10 The U.S. Government may have rights in the present invention pursuant to the
terms of grant numbers AR40780-8 and AR42671-05 awarded by the National
Institutes of Health and DARPA/AFOSR grant number F49620-98-1-0487.

FIELD OF THE INVENTION

15 The present invention relates to the growth of cells in culture. More
particularly, the present invention provides methods and compositions for increasing
cell survival, cell proliferation and/or cell differentiation along specific pathways by
growing the cells in low ambient oxygen conditions.

BACKGROUND OF THE INVENTION

20 In a time of critical shortages of donor organs, efforts to bring cellular
transplantation into the clinical arena are urgently needed (Neelakanta & Csete,
1996). Indeed, cellular and tissue transplantation is now well recognized as a
desirable technique for the therapeutic intervention of a variety of disorders including
cystic fibrosis (lungs), kidney failure, degenerative heart diseases and
neurodegenerative disease. However, although this may be a desirable and much
needed intervention, a major impediment to this type of therapeutic intervention is the
lack of an available supply of viable, differentiated cells. Generally differentiated
25 cells cannot be readily expanded in culture. Thus, methods of increasing the number
and/or availability of differentiated, viable cells are needed.

The central nervous system (CNS) (brain and spinal cord) has poor
regenerative capacity which is exemplified in a number of neurodegenerative

L7 ANSWER 45 OF 108 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2000:351640 CAPLUS
 DOCUMENT NUMBER: 132:331683
 TITLE: Low oxygen culturing of neural crest stem cells
 INVENTOR(S): Ceste, Marie; Doyle, John; Wold, Barbara J.; Morrison, Sean J.; Anderson, David
 PATENT ASSIGNEE(S): California Institute of Technology, USA
 SOURCE: PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029549	A2	20000525	WO 1999-US27532	19991118
WO 2000029549	A3	20011011		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6184035	B1	20010206	US 1998-195569	19981118
EP 1144591	A2	20011017	EP 1999-961727	19991118
EP 1144591	A3	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002530067	T2	20020917	JP 2000-582533	19991118
US 2001034061	A1	20011025	US 2001-773824	20010131
US 6589728	B2	20030708		

PRIORITY APPLN. INFO.:
 US 1998-195569 A 19981118
 US 1999-425462 A 19991022
 WO 1999-US27532 W 19991118

AB The present invention relates to the growth of cells in culture under conditions that promote cell survival, proliferation, and/or cellular **differentiation**. The present inventors have found that proliferation was promoted and apoptosis reduced when cells were grown in lowered oxygen as compared to environmental oxygen conditions traditionally employed in cell culture techniques. Further, the inventors found that **differentiation** of precursor cells to specific fates also was enhanced in lowered oxygen where a much greater no. and fraction of **dopaminergic** neurons were obtained when mesencephalic precursors were expanded and **differentiated** in lowered oxygen conditions. Thus at more physiol. oxygen levels the proliferation and **differentiation** of **CNS** precursors is enhanced, and lowered oxygen is a useful adjunct for ex vivo generation of specific neuron types. Methods and compns. exploiting these findings are

L7 ANSWER 70 OF 108 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 32

ACCESSION NUMBER: 1999:204384 CAPLUS

TITLE: Transplantation of expanded mesencephalic precursors leads to recovery in parkinsonian rats

AUTHOR(S): Studer, Lorenz; Tabar, Viviane; McKay, Ron D. G.

CORPORATE SOURCE: Laboratory of Molecular Biology, NINDS, NIH, Bethesda, MD, 20892, USA

SOURCE: Nature Neuroscience (1998), 1(4), 290-295

CODEN: NANEFN; ISSN: 1097-6256

PUBLISHER: Nature America

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In vitro expansion of **central nervous system**

(**CNS**) precursors might overcome the limited availability of **dopaminergic** neurons in transplantation for Parkinson's disease, but generating **dopaminergic** neurons from in vitro dividing precursors has proven difficult. Here a three-dimensional cell **differentiation** system was used to convert precursor cells derived from E12 rat ventral mesencephalon into **dopaminergic** neurons. We demonstrate that **CNS** precursor cell populations expanded in vitro can efficiently **differentiate** into **dopaminergic** neurons, survive intrastriatal transplantation and induce functional recovery in hemiparkinsonian rats. The numerical expansion of primary **CNS** precursor cells is a new approach that could improve both the ethical and the tech. outlook for the use of human fetal tissue in clin. transplantation.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 71 OF 108 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:200005 BIOSIS
DOCUMENT NUMBER: PREV199900200005
TITLE: Transplantation of expanded mesencephalic precursors leads
to recovery in parkinsonian rats.
AUTHOR(S): Studer, Lorenz; Tabar, Viviane; McKay, Ron D. G. (1)
CORPORATE SOURCE: (1) Laboratory of Molecular Biology, NINDS, NIH, 36 Convent
Drive, Building 36, Room 5A29, Bethesda, MD, 20892 USA
SOURCE: Nature Neuroscience, (July, 1998) Vol. 1, No. 3, pp.
290-295.
ISSN: 1097-6256.
DOCUMENT TYPE: Article
LANGUAGE: English

AB In vitro expansion of **central nervous system**
(**CNS**) precursors might overcome the limited availability of
dopaminergic neurons in transplantation for Parkinson's disease,
but generating **dopaminergic** neurons from in vitro dividing
precursors has proven difficult. Here a three-dimensional cell
differentiation system was used to convert precursor cells derived
from E12 rat ventral mesencephalon into **dopaminergic** neurons. We
demonstrate that **CNS** precursor cell populations expanded in
vitro can efficiently **differentiate** into **dopaminergic**
neurons, survive intrastriatal transplantation and induce functional
recovery in hemiparkinsonian rats. The numerical expansion of primary
CNS precursor cells is a new approach that could improve both the
ethical and the technical outlook for the use of human fetal tissue in
clinical transplantation.

ACCESSION NUMBER: 1997:749652 CAPLUS

DOCUMENT NUMBER: 128:73376

TITLE: Involvement of protease-activated receptor-1 in the in vitro development of mesencephalic dopaminergic neurons

AUTHOR(S): Debeir, Th.; Benavides, J.; Vige, X.

CORPORATE SOURCE: Synthelabo Recherche CNS Research Department, Bagneux, 92225, Fr.

SOURCE: Neuroscience (Oxford) (1997), Volume Date 1998, 82(3), 739-752

CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In situ hybridization studies have revealed high levels of protease (thrombin)-activated receptor-1 mRNA in the mesencephalon of rats, suggesting that **dopaminergic** neurons are a target for thrombin's actions. We have evaluated the effect of thrombin receptor activation, either by thrombin or by thrombin receptor agonist peptide, a 14 amino acid agonist of protease-activated receptor-1, on tyrosine hydroxylase-pos. neurons. Pure cultures of rat mesencephalic neurons or co-cultures of mesencephalic neurons and glial cells were treated with either thrombin or thrombin receptor agonist peptide the day after plating. Tyrosine hydroxylase-pos. cell counting, [3H]dopamine uptake and morphometric anal. were performed on day 5. Thrombin and thrombin receptor agonist peptide influenced neurite elongation, branching and the no. of primary, secondary and tertiary neurites of tyrosine hydroxylase-pos. neurons. In pure cultures, the most significant effects of thrombin and thrombin receptor agonist peptide were to delay branching and to increase the centrifugal growth of neurites without affecting the total neuritic length. Thrombin (up to 10 nM) and thrombin receptor agonist peptide did not affect the no. of tyrosine hydroxylase-pos. neurons or [3H]dopamine uptake. Neurotrophin-4 also influenced the morphol. of tyrosine hydroxylase-pos. neurons. The increase of neuritic length initiated by this neurotrophin is complementary to the radial elongation induced by protease-activated receptor-1 activation. When neurons were cultured in the presence of glial cells, the effects of thrombin and thrombin receptor agonist peptide on most of these parameters were larger than those obsd. with pure cultures. Thus, thrombin is able to initiate a complex remodeling of the architecture of tyrosine hydroxylase-

L7 ANSWER 78 OF 108 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 ACCESSION NUMBER: 1998015422 EMBASE
 TITLE: Neurotrophic factors and neurodegenerative diseases.
 AUTHOR: Scarlato G.; Ntanos I.; Bernasconi S.
 CORPORATE SOURCE: I. Ntanos, Pneumological Clinic, University of Athens,
 Sotiria Hospital, Athens, Greece
 SOURCE: Neurologia Psichiatria Scienze Umane, (1997) 17/4
 (511-517).
 Refs: 4
 ISSN: 1120-2254 CODEN: NPSUEU
 COUNTRY: Italy
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English; Italian

AB Neurotrophic factors (NTFs), necessary for the maintenance of structural integrity and the regulation of plasticity of the adult brain, may become involved at diverse levels during neurodegeneration. The phenotypes of many neurodegenerative diseases, including Amyotrophic Lateral Sclerosis (ALS), Alzheimer disease (AD), and Parkinson disease (PD) are determined by the vulnerability of specific populations of neurons in the **central nervous system (CNS)**. The concept that NTFs may become useful to treat neurodegeneration was based on the hypothesis that reduced availability of target-derived neurotrophic factors may lead to the loss of the innervating neuronal populations and that NTFs would act to prevent neuronal dysfunction and death of these neurons selectively degenerated. NGF has been proposed as therapeutic treatment for AD, a disease characterized by the loss of cholinergic neurons, because NGF acts in a trophic way on these cells. Concerning Parkinson disease, bFGF, Insulin-like Growth Factor-1/2 (IGF1/IGF- 2), Epidermal Growth Factor (EGF), Transforming Growth Factor alfa (TGF- alfa) and BDNF are factors able to promote **differentiation** of the mesencephalic **dopaminergic** neurons. In ALS Ciliary Neurotrophic Factor (CNTF), Neurotrophins 4/5 (NT 4/5) and Glial Cell Line Derived Neurotrophic Factor (GDNF) have been shown to have trophic effects on the motor neurons.

L7 ANSWER 86 OF 108 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 43

ACCESSION NUMBER: 1994:318641 BIOSIS

DOCUMENT NUMBER: PREV199497331641

TITLE: Intracerebral transplantation: Basic and clinical
applications to the neostriatum.

AUTHOR(S): Fisher, Lisa J.; Gage, Fred H. (1)

CORPORATE SOURCE: (1) Dep. Neurosciences, Clinical Sciences Bldg., Univ.
Calif. San Diego, 9500 Gilman Drive, La Jolla, CA
92093-0627 USA

SOURCE: FASEB Journal, (1994) Vol. 8, No. 8, pp. 489-496.
ISSN: 0892-6638.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Many studies have used the intracerebral transplantation technique to study the neostriatum. Most of this work has been conducted in two well-characterized animal models of striatal dysfunction: the rat model of Huntington's disease (striatal damage) and the rat model of Parkinson's disease (damage of **dopaminergic** nigrostriatal afferents). In animals with striatal damage, fetal striatal tissue implanted into the neostriatum (homotypic transplants) displays a remarkable anatomical and functional incorporation into the host brain. These homotypic grafts also induce a wide range of behavioral improvements in experimental animals. In contrast, fetal substantia nigra neurons implanted into the dopamine-depleted neostriatum (heterotypic transplants) generally show a more restricted integration into the host brain and elicit fewer behavioral improvements. Nonetheless, the ability of grafted fetal neurons to survive, **differentiate**, and partially reconstruct an appropriate and functional neurocircuitry with host systems indicates that there are factors within the adult brain that promote neuronal development and regeneration. Such results have encouraged the clinical use of intracerebral grafts for the treatment of Parkinson's disease. Recent studies have emphasized the use of genetically modified cells and neural cell lines as alternative populations to study and repair the **central nervous system**.

L7 ANSWER 87 OF 108 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 44

ACCESSION NUMBER: 1994:479935 BIOSIS

DOCUMENT NUMBER: PREV199497492935

TITLE: The response of human and rat fetal ventral mesencephalon
in culture to the brain-derived neurotrophic factor
treatment.

AUTHOR(S): Zhou, Jiawei (1); Bradford, Henry F.; Stern, Gerald M.

CORPORATE SOURCE: (1) Dep. Biochem., Imperial Coll. Sci. Technol. and Med.,
Imperial College Road, London SW7 2AY UK

SOURCE: Brain Research, (1994) Vol. 656, No. 1, pp. 147-156.
ISSN: 0006-8993.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Brain-derived neurotrophic factor (BDNF) has been shown to increase the survival of **dopaminergic** neurons in rodent mesencephalic cultures. The mRNAs of BDNF and trk B receptor have been found to be expressed in the substantia nigra of rat. In this study, the action of BDNF was studied on the survival and transmitter-specific **differentiation** of **dopaminergic** neurons of fetal human **CNS** aged 9-10-week in vitro. **Dopaminergic** neuron viability and phenotypic expression were monitored by tyrosine hydroxylase (TH) immunohistochemistry and measurement of dopamine (DA) content with HPLC, respectively. After seven days of treatment with BDNF there were 2.2-fold greater number of TH+ neurons surviving than in untreated cultures. Although very low levels of DA were detectable in human tissue, considerable amounts of DA was found in the culture medium from around 13 days in vitro (DIV), indicating that DA in human fetal tissue tended to be synthesized and released into the incubation medium more readily than from cultured rat fetal tissue during the same period. The content of DA in the BDNF-treated cultures was approximately double that of untreated cultures after 7 days. In rat fetal tissue, the capacity of each TH+ neuron to produce DA was not changed in the BDNF-treated cultures (7 DIV) compared with control cultures, suggesting that BDNF does not up-regulate the production of DA but rather acts to reduce cell death rates. Ciliary neurotrophic factor (CNTF) treatment of rat mesencephalic culture failed to improve the period of survival of fetal **dopaminergic** neurons and had no effect on the production of DA in cultures. Taken together, our results suggest that BDNF has potent trophic effect on both rat and human fetal mesencephalic **dopaminergic** neurons in culture and has a potential application in the treatment of Parkinson's disease.

7 ANSWER 89 OF 108 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1993:642038 CAPLUS

DOCUMENT NUMBER: 119:242038

TITLE: IGF-I supports the survival and/or differentiation of multiple types of central nervous system neurons

AUTHOR(S): Bozyczko-Coyne, Donna; Glicksman, Marcie A.; Prantner, J. Eric; McKenna, Beth; Connors, Tom; Friedman, Connie; Dasgupta, Malini; Neff, Nicola T.

CORPORATE SOURCE: Cephalon, Inc., West Chester, PA, 19380, USA

SOURCE: Annals of the New York Academy of Sciences (1993), 692(Role of Insulin-like Growth Factors in the Nervous System), 311-13

CODEN: ANYAA9; ISSN: 0077-8923

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To identify addnl. cellular targets of IGF-I in the **CNS** and to more fully characterize its potential survival and **differentiation** activities, IGF-I effects on a variety of neurons derived from the **CNS** were examd. IGF-I was shown to promote survival of primary cultured embryonic brain neurons. In addn., results suggest that IGDF-I promotes the rate of **differentiation** and/or the survival of cholinergic and **dopaminergic** neurons. IGF-I might also act on these neuronal populations to recruit addnl. neurons to a cholinergic of **dopaminergic** phenotype via phenotypic switching.

L7 ANSWER 97 OF 108 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 50

ACCESSION NUMBER: 1988:26011 BIOSIS

DOCUMENT NUMBER: BA85:13736

TITLE: DOPAMINERGIC NEURONS FROM EMBRYONIC MOUSE MESENCEPHALON ARE
ENRICHED IN CULTURE THROUGH IMMUNOREACTION WITH MONOCLONAL
ANTIBODY TO NEURAL SPECIFIC PROTEIN 4 AND FLOW CYTOMETRY.

AUTHOR(S): DI PORZIO U; ROUGON G; NOVOTNY E A; BARKER J L

CORPORATE SOURCE: LAB. NEUROPHYSIOL., NATL. INST. NEUROL. COMMUNICATIVE
DISORD. STROKE, NATL. INST. HEALTH, BETHESDA, MD. 20892,
USA.

SOURCE: PROC NATL ACAD SCI U S A, (1987) 84 (20), 7334-7338.
CODEN: PNASA6. ISSN: 0027-8424.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB **Dopaminergic** neurons represent a rare neurotransmitter phenotype
within the mammalian **central nervous system**.

The mesencephalic **dopaminergic** neurons form the ascending
dopaminergic pathways in mammals and are involved in motor and
limbic functions. Here we report that about 30% of all developing mouse
mesencephalic cells, including virtually all of the **dopaminergic**
phenotype, express surface membrane determinant(s) recognized by a
monoclonal antibody to neural specific protein 4 (NSP4). We have been
able to isolate and culture neurons from the mesencephalon according to
their expression of NSP4, using the anti-NSP4 immunoreaction in
conjunction with fluorescence-activated cell sorting. Cultures of
NSP4+-sorted cells showed a significant enrichment in three
morphologically distinct putative **dopaminergic** phenotypes when
compared to unsorted mesencephalic cultures, whereas the cultures of
NSP4--sorted cells were virtually devoid of **dopaminergic**
neurons. This flow cytometric enrichment in **dopaminergic**
neurons should provide the necessary cells for multidisciplinary study of
dopaminergic phenotype **differentiation**.

> d his

(FILE 'HOME' ENTERED AT 15:23:52 ON 05 SEP 2003)

FILE 'BIOSIS, EMBASE, CAPLUS, MEDLINE' ENTERED AT 15:24:07 ON 05 SEP 2003

L1 2113 S DIFFERENTIATED NEURON?
L2 333750 S CELL CULTURE
L3 39 S L1 (P) L2
L4 18 DUPLICATE REMOVE L3 (21 DUPLICATES REMOVED)
E STUDER
E STUDER/IN
E STUDER L/IN
E STUDER L/AU
L5 0 S E3 AND E4 AND E5 AND E6 AND E9
L6 141 S E3 OR E4 OR E5 OR E6 OR E9
L7 73 DUPLICATE REMOVE L6 (68 DUPLICATES REMOVED)
L8 1005874 S NEURON?
L9 41 S L7 AND L8

FILE 'STNGUIDE' ENTERED AT 15:56:47 ON 05 SEP 2003

=> log y

L9 ANSWER 21 OF 41 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:200005 BIOSIS

DOCUMENT NUMBER: PREV199900200005

TITLE: Transplantation of expanded mesencephalic precursors leads to recovery in parkinsonian rats.

AUTHOR(S): Studer, Lorenz; Tabar, Viviane; McKay, Ron D. G.
(1)

CORPORATE SOURCE: (1) Laboratory of Molecular Biology, NINDS, NIH, 36 Convent Drive, Building 36, Room 5A29, Bethesda, MD, 20892 USA

SOURCE: Nature Neuroscience, (July, 1998) Vol. 1, No. 3, pp. 290-295.

ISSN: 1097-6256.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In vitro expansion of central nervous system (CNS) precursors might overcome the limited availability of dopaminergic **neurons** in transplantation for Parkinson's disease, but generating dopaminergic **neurons** from in vitro dividing precursors has proven difficult. Here a three-dimensional cell differentiation system was used to convert precursor cells derived from E12 rat ventral mesencephalon into dopaminergic **neurons**. We demonstrate that CNS precursor cell populations expanded in vitro can efficiently differentiate into dopaminergic **neurons**, survive intrastriatal transplantation and induce functional recovery in hemiparkinsonian rats. The numerical expansion of primary CNS precursor cells is a new approach that could improve both the ethical and the technical outlook for the use of human fetal tissue in clinical transplantati

L9 ANSWER 24 OF 41 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:512383 BIOSIS
DOCUMENT NUMBER: PREV199699234739
TITLE: Noninvasive dopamine determination by reversed phase HPLC
in the medium of free-floating roller tube cultures of rat
fetal ventral mesencephalon: A tool to assess dopaminergic
tissue prior to grafting.
AUTHOR(S): **Studer, L.**; Psylla, M.; Buehler, B.; Evtouchenko,
L.; Vouga, C. M.; Leenders, K. L.; Seiler, R. W.; Spenger,
C. (1)
CORPORATE SOURCE: (1) Dep. Neurosurgery, Univ. Bern, Inselspital, CH-3010
Bern Switzerland
SOURCE: Brain Research Bulletin, (1996) Vol. 41, No. 3, pp.
143-150.
ISSN: 0361-9230.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The low availability of dopamine containing **neurons** for grafting
in Parkinson's disease is a general problem. Free-floating roller tube
(FFRT) cultures allow storage of fetal mesencephalic tissue prior to
transplantation. Preoperative functional testing permits to select an
optimized set of individual cultures for transplantation. Rat fetal
ventral mesencephali (E13) were dissected out and divided into four
equally sized pieces each and individually prepared as FFRT cultures.
After 4, 8, 12, and 16 days in vitro (DIV) the medium of each culture was
collected during routine medium change and immediately stabilized.
Dopamine was extracted and probes were determined with reversed phase HPLC
using electrochemical detection. After 16 DIV cultures were fixed and cell
counts performed in tyrosine hydroxylase (TH)-immunostained serial
sections. The mean dopamine content \pm SEM in culture conditioned media
was at 4 DIV: 21 ± 2 pg, $n = 38$; at 8 DIV: 37 ± 4 pg, $n = 40$; at 12 DIV:
 52 ± 7 pg, $n = 38$; and at 16 DIV: 39 ± 5 pg, $n = 38$. In all cultures
devoid of dopamine after 4 and 8 DIV (12.5%) levels remained below
detectability at 12 and 16 DIV. Cultures derived from the rostral
mesencephalon showed significantly higher dopamine values than those from
the caudal mesencephalon at 12 DIV. The mean number of TH-immunoreactive
(-ir) cells/culture \pm SEM after 16 DIV was 556 ± 51 , $n = 40$. The
correlation between TH-ir cell number (CN) and dopamine content of
rostrally derived cultures at 16 DIV was: $CN = 7.4 (\text{dopamine (pg)}) + 248$;
 $R = 0.75$; $n = 19$; $p < 0.001$. No dopamine was present in cultures without
TH-ir cells. These results demonstrate that sequential noninvasive
screening of dopamine in single cultures is feasible and that the dopamine
content is correlated to the number of surviving TH-ir cells. This permits
to select cultures rich in dopaminergic **neurons** for
transplantation.

9 ANSWER 25 OF 41 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:231324 BIOSIS
DOCUMENT NUMBER: PREV199698795453
TITLE: Effects of brain-derived neurotrophic factor on

neuronal structure of dopaminergic **neurons**
in dissociated cultures of human fetal mesencephalon.
AUTHOR(S): **Studer, Lorenz**; Spenger, Christian (1); Seiler,
Rolf W.; Lindvall, Agneta Othberg Olle; Odin, Per
CORPORATE SOURCE: (1) Dep. Neurosurgery, Univ. Bern, Inselspital, CH-3010
Bern Switzerland
SOURCE: Experimental Brain Research, (1996) Vol. 108, No. 2, pp.
328-336.
ISSN: 0014-4819.

DOCUMENT TYPE: Article
LANGUAGE: English

AB Brain-derived neurotrophic factor (BDNF) has been shown to promote the survival of cultured fetal mesencephalic dopaminergic **neurons** of rat and human origin. In the present study, BDNF was tested for its ability to influence **neuronal** structure of dopaminergic **neurons** in dissociated cultures of human fetal ventral mesencephalon after 7 days in vitro. Following immunocytochemical staining for tyrosine hydroxylase, all surviving dopaminergic **neurons** were counted. Computer-assisted three-dimensional reconstructions of uniform randomly selected **neurons** cultured with 50 ng/ml BDNF (n=120) or without BDNF (n=80) were made. BDNF increased the number of surviving human dopaminergic **neurons** by 76%. Mean soma profile area was significantly enlarged by 18% in BDNF-treated **neurons** as compared to controls. Analysis of parameters of neuritic size and complexity in these cultures revealed that combined neuritic length, combined neuritic volume, and neuritic field area were increased by 60%, 125% and 129%, respectively, and the mean number of segments per cell was increased by 41%. A change in neurite complexity in BDNF-treated cultures was further confirmed by the Sholl's concentric sphere analysis. These results demonstrate that BDNF promotes development and differentiation of human fetal dopaminergic **neurons** in vitro.